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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/624,965	07/25/2000	Colin Louis Masters	9287ZY	7006

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EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	14

DATE MAILED: 02/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/624,965	Applicant(s) MASTERS ET AL.	
	Examiner Olga N. Chernyshev	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 28-33 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 28-33 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. It has been understood that Applicant has intended to amend claims 28 and 31, not claims 28 and 30. Claims 28 and 31 have been amended as requested in the amendment of Paper No.13, filed on December 10, 2001. Claims 28-33 are pending in the instant application.

2. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on December 10, 2001 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

5. Claims 28-33 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant argues that the instant specification is fully enabled and provides a copy of a declaration by C. L. Masters filed under 37 C. F. R. § 1.132 in parent application number 08/757,537. The Examiner has carefully reviewed the information contained in the declaration; however, it was found insufficient to overcome the rejection for the following reasons. Applicant

refers to the part of the declaration where "zinc loading experiments in rats resulted in elevated levels of full length APP and reduced levels of soluble APP compared to control" (page 7, second paragraph of the Response). According to Applicant, these experiments provided "actual experimental evidence" of the "effect of zinc on APPase-mediated cleavage" (page 7). The Examiner disagrees with such interpretations of the data and refers to the section 7, second paragraph of the previous office action. Briefly, it is well recognized in the art that normal function of APP is being a neurotrophic factor, among others. That is why the initial elevation of APP might just as well be a part of a normal response to elevated concentration of zinc and in fact may be the beginning of a process of damage repair, which is a normal function of APP. Moreover, there is no evidence presented in the study that the decreased levels of zinc in the diet would be beneficial to the animals in such experimental conditions.

Applicant submits further that the absence of working examples in the instant application cannot prevent a skilled artisan to practice the full scope of the invention as claimed (page 7, last paragraph). The Examiner disagrees, first, that the instant specification "provides adequate teaching to support the claimed invention" and, second, maintains the requirement for working examples based on the well-known unpredictability of art of possible treatment for Alzheimer's disease (AD). See *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970), which held that

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35

U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved"(emphasis added by the Examiner). Applicant's reference to the parent application on page 8, first paragraph is moot in view of the fact that the application was abandoned during the prosecution.

Applicant argues that the data presented in the declaration showed that amounts of insoluble amyloid Aβ plaques in Tg2576 transgenic mice treated with a metal chelator clioquinol were decreased compared to the placebo controls and animal's behavior improved (page 8, second paragraph). The Examiner agrees with the Applicant's statement that Tg2576 is a recognized animal model for Alzheimer's disease. However, it is also well recognized in the art that this model has its limitations. Tg2567 mice develop Alzheimer's-like Aβ brain deposits because of overexpression of a human amyloid precursor protein (APP) transgene with a double mutation found in a Swedish (APP swe) family early onset AD (see Pratico et al., p.4183, first column, second paragraph). Genetic, i.e., due to a known gene mutation, nature of AD accounts only for a very small number of known AD cases (see Clark et al., p.286, Figure11.1). Thus, in most cases etiology of AD remains unclear, and is not due to the overexpression of APP. Therefore, it is the Examiner's position that the results of the experiments obtained on transgenic

Tg2576 mice cannot be simply extrapolated and generally applied to humans. Decrease in amyloid plaque formation in mice with altered genotype cannot be considered as "successful treatment by cessation of typical symptoms" (page 8, third paragraph of the Response) and, consequently, treatment with metal chelators cannot readily be used for a treatment of AD. The Examiner also strongly disagrees with Applicant's position that "Dosing and relief or disappearance of symptoms are part of any treatment of any ailment" (page 8). First, the "disappearance" of amyloid plaques was never shown in presented experiments. Second, "dosing", or claimed "therapeutically effective amount" (claims 28, 30) is a part of the invention and must be present in the specification in order to provide one skilled in the art with precise protocol how to practice the claimed invention. To practice such a method would require knowledge of the route, duration and quantity of administration of the factor to a subject and this information is not provided by the instant specification. The instant specification has also failed to disclose how these parameters are to be determined, how a similar method was practiced in the art with a different agent or to provide even a single working example, prophetic or actual, of the claimed method. In the absence of this guidance a practitioner would have to resort to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of therapeutically effective amount of an agent of the instant invention. The instant situation is directly analogous to that which was addressed in *In re Colianni*, 195 U.S.P.Q. 150,(CCPA 1977), which held that a "[d]isclosure that calls for application of "sufficient" ultrasonic energy to practice claimed method of fusing bones but does not disclose what "sufficient" dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequence, and duration, and contains no specific examples or

embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. 112 first paragraph".

New ground of rejection.

6. Claims 28-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The last amendment of the claims 28 and 31 has introduced a new matter into the claims by excluding EDTA from the list of agents "capable of crossing the blood brain barrier, wherein said agent modulates the interaction within the central nervous system between a divalent or trivalent cation and/or heparin with amyloid precursor protein" (claim 28). The instant specification does not provide adequate support or written description for such limitation. Any negative limitation or exclusionary proviso must have basis in the original disclosure. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. Note that a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a prima facie case for lack of descriptive support. Ex parte Parks, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993). See MPEP § 2163 - § 2163.07(b) for a discussion of the written description requirement of 35 U.S.C. 112, first paragraph. See MPEP 2173.05 (i).

Conclusion

7. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax

center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
February 15, 2002 OC

JOHN ULM
PRIMARY EXAMINER
GROUP 1800